Solubilities of Fatty Acids and Derivatives in Acetone[1]

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KNOWLEDGE of the solubilities of fatty acids and derivatives in organic solvents at various temperatures is useful in the research laboratory and in industry in connection with low-temperature fractional crystallization and liquid-liquid distribution processes. The presently available information has been covered quite completely in two reviews (1, 2). It is characterized by many gaps, largely for two reasons: a) many of the compounds are difficult to prepare in sufficiently pure form, and b) technical problems introduced by such phenomena as polymorphism and supercooling sometimes make reliable measurements difficult.

In previous measurements, two methods have been used to determine solubilities. Brown et al. (2, 3) and Bailey et al. (1) have used a so-called analytical method, which involves withdrawal and analysis of a portion of a solution in which equilibrium has been established between the solvent phase and an excess of solute. Others have used a "synthetic" method, which is somewhat simpler and has the added advantage of using appreciably less material without sacrifice of accuracy. This method consists of observing the temperature at which the last crystal disappears when raising the temperature of a solution of known gross composition or, alternatively, of observing the temperature at which the first crystal appears when the temperature is lowered. Hoerr and Harwood (5) employed the rising temperature technique. Ward and Singleton (11), using the falling temperature method, introduced refinements involving an examination of the cooling curves at different rates of cooling. This permitted corrections for the effects of supercooling and eliminated the necessity for visual detection of crystal formation. Using a sensitive potentiometer-galvanometer system, which detected temperature changes of the order of 0.001°C., they were able to measure accurately solubilities of 1-monostearin in the range of 0.1 to 0.2%.

The method used in our investigation was essentially an adaptation of that used by Hoerr and Harwood (5). The study was undertaken to fill gaps in the information available about solubilities in acetone for saturated fatty acids with even numbers of carbon atoms from C_6 to C_{18} oleic, linoleic, and linolenic acids, and methyl esters, alcohols, and simple triglycerides derived from these fatty acids.

Materials

Saturated Acids and Methyl Esters. The starting materials for the preparation of purified caproic, caprylic, capric, lauric, and myristic acids were commercial grades of the free acids. The acids were esterified with methanol, using sulfuric acid as catalyst. The esters were purified by repeated distillations of center cuts through a 4-ft. Podbielniak Hyper-Cal

column. Purified acids were obtained through saponification of portions of the purified esters.

Palmitic acid and methyl palmitate were derived from virgin olive oil (pressed). The C_{16} acid fraction of the methyl esters of the olive oil fatty acids was separated by fractional distillation and hydrolyzed. The free acids were recrystallized six times from ethyl alcohol. A portion of the purified acid was esterified with methanol, using sulfuric acid as catalyst, and the product was distilled to yield methyl ester.

The purified stearic acid and methyl stearate were prepared from a commercial stearic acid (Hystrene S-97, Atlas Powder Company). The crude acid was converted to the lead salt, and unsaturated impurities were removed by the method of Philipson et al. (9). The free acid was regenerated, esterified with methanol, and fractionally distilled. The constant boiling ester fraction of the C_{18} acids was purified further by crystallization from diethyl ether. The final stearic acid was then obtained through saponification of a portion of the purified ester. Analytical data on the purified saturated acids and esters are given in Table I. Melting points were determined by the capillary method.

Unsaturated Acids and Methyl Esters. Virgin olive oil (pressed) was used as a starting material for the preparation of oleic acid and methyl oleate. The methyl esters of the C_{18} acid fraction of olive oil methyl esters was obtained by fractional distillation. Methyl oleate was obtained from these esters by repeated low temperature-fractional crystallizations from acetone and was fractionally distilled for further purification. Purified oleic acid was obtained through saponification of a portion of the purified ester. Analytical values for the purified ester were as follows: iodine value (Wijs) 86.0, n_D^{40} 1.4445.

Linoleic acid and methyl linoleate were derived from safflower oil fatty acids. The linoleic acid was

TABLE I
Physical Properties of Normal Saturated Compounds

Substance	Melting point (capillary method) (°C.)	Refractive index (°C.)
Caproic acid	−3.5	1.4170/20
Caprylic acid	16.2	1.4241/30
Capric acid	30.4	1.4287/40
Lauric acid	44.2	1.4328/45.3
Myristic acid	54.4	1.4329/55
Methyl caproate	......	1.3990/35
Methyl caprylate	......	1.4152/25
Methyl caprate	......	1.4239/25
Methyl laurate	......	1.4303/25
Methyl myristate	......	1.4350/25
Methyl palmitate	30.4–30.5	1.4359/35
Methyl stearate	38.5–38.9	1.4370/40
Caproyl alcohol	−47.7 to −47.2	1.4184/20
Caprylyl alcohol	−15.2	1.4292/20
Capryl alcohol	6.9	1.4372/20
Lauryl alcohol	24.5	1.4374/25
Myristyl alcohol	37.5	1.4347/50
Palmityl alcohol	49.3	1.4394/51.5
Stearyl alcohol	58.1	1.4390/60
Tricaproin	......	1.4431/25
Tricaprylin	......	1.4480/20
Tricaprin	29.0	1.4451/40
Trilaurin	43.0–43.5	1.4401/60
Trimyristin	54.0–55.0	1.4420/60
Tripalmitin	66.5	1.4387/80
Tristearin	70.0–71.0	1.4403/80

concentrated by urea fractionation of the safflower oil acids and was further purified by repeated low-temperature crystallizations from Skellysolve F. The concentrate was esterified with methanol, and the esters were fractionally distilled. A portion of the purified linoleate from the center cut was saponified to obtain a purified linoleic acid. Analytical values for the purified methyl linoleate were as follows: iodine value (Wijs) 171.6, n_D^{25} 1.4695.

Linolenic acid and methyl linolenate were prepared by the method of Mathews, Brode, and Brown (8) from linolenic acid derived from linseed oil by a bromination-debromination procedure. After 12 recrystallizations from Skellysolve F at −65°C., the linolenic acid had the following analytical values: iodine value (Wijs) 273.2, n_D^{20} 1.4805; m.p. −11.3 to −11.2°C.; conjugated diene by ultraviolet analysis 0.12%.

Because the linolenic acid showed a slight absorption at 10.33 μ in the infrared spectral region, the product was recrystallized an additional 14 times from Skellysolve F at −65°C. The slight absorption at 10.33 μ persisted and very probably was caused by trans isomers; the absorption was too small however to permit accurate determination of the amount of contamination with trans material.

A portion of the purified linolenic acid was esterified with methanol, and a purified methyl linolenate was obtained by simple distillation of the product.

Saturated Alcohols. Commercial samples of good quality were used as source materials. These were further purified by careful fractional distillation and, wherever necessary, this was followed by fractional crystallization from acetone to yield the final products. Analytical values for the unsaturated alcohols are given in Table I.

Unsaturated Alcohols. Oleyl (iodine value 93.6, n_D^{25} 1.4580), linoleyl (iodine value 186.6, n_D^{30} 1.4676), and linolenyl (iodine value 288.0, n_D^{30} 1.4778) alcohol were prepared by lithium aluminum hydride reduction of the corresponding purified fatty acids by the method of Ligthelm et al. (7). On infrared spectrophotometric examination, carbonyl impurities could not be detected in the final products, but a small amount of isomers containing trans double bonds was present in the linolenyl alcohol. Conjugated diene by ultraviolet analysis was virtually nil in the final products.

Triglycerides. The triglycerides of the saturated fatty acids from C_{14} to C_{18} and of the unsaturated fatty acids were prepared by trans-esterification of the methyl esters with triacetin, using sodium methoxide as catalyst. Soap, mono- and diglycerides, and

TABLE II

Solubility Data
(g. solute per 100 g. of solvent/°C.)

Caproic acid	Caprylic acid	Capric acid	Lauric acid	Myristic acid	Linoleic acid	Linolenic acid
91.6 /−31.7	138.7 /−4.9	106.5 /6.2	22.8 /8.6	16.8 /21.3	11.49/−37.3	45.1 /−36.9
60.3 /−38.8	84.2 /−11.2	64.2 /0.6	9.84/0.6	7.51/13.0	5.47/−44.4	25.8 /−41.3
38.5 /−46.9	62.3 /−15.4	28.6 /−7.2	6.94/−3.5	3.27/5.1	2.00/−52.1	11.4 /−49.3
24.4 /−56.6	56.1 /−17.4	11.8 /−18.9	2.05/−18.1	0.91/−9.0	0.69/>−79.3	7.79/−53.8
11.6 /−70.0	59.4 /−19.3	5.55/−29.0	0.59/−31.4	0.53/−12.3	0.52/<−79.3	5.66/−56.3
	37.2 /−22.5	2.65/−38.7	0.20/−42.9	0.18/−25.3		3.22/−62.3
	21.5 /−30.7	1.11/−50.5		0.05/<−79.3		2.73/−66.9
	9.42/−48.5	0.58/−54.5				1.04/>−79.3
	4.24/−58.6					0.77/<−79.3

Methyl caproate [a]	Methyl caprylate	Methyl caprate	Methyl laurate	Methyl myristate	Methyl palmitate	Methyl stearate
400.0 /−76.0	330.0 /−44.3	330.0 /−20.0	37.2 /−13.3	32.0 /0.5	33.0 /12.3	5.93/13.0
100.0 /−86.0	43.7 /−58.0	96.4 /−27.0	10.68/−21.5	11.1 /−6.3	10.80/6.5	1.10/ 1.5
42.8 /−93.0	18.1 /−65.5	43.4 /−31.8				
21.2 /−100.0	8.72/>−79.3	25.1 /−35.3				
5.27/−120.0	5.74/<−79.3	18.1 /−37.5				
		11.6 /−41.8				
		5.49/−49.5				
		1.21/>−79.3				
		0.21/<−79.3				

Methyl oleate	Methyl linoleate	Methyl linolenate	Caproyl alcohol	Caprylyl alcohol	Capryl alcohol	Lauryl alcohol
208.0 /−27.5	200.0 /−45.7	192.0 /−62.3	834.0 /−49.3	14.8 /−34.8	15.7 /−15.2	14.7 /0.8
98.0 /−29.4	104.0 /−47.5	101.0 /−64.7	225.0 /−52.2	9.08/−39.5	6.77/−22.3	7.43/−4.8
44.9 /−31.0	48.4 /−49.8	47.9 /−68.0	66.7 /−56.0	4.89/−46.8	3.12/−28.1	4.48/−9.5
27.1 /−33.0	26.1 /−51.7	28.2 /−69.8	25.3 /−59.8	1.43/−60.1	1.51/−36.1	1.54/−20.3
12.0 /−35.3	11.5 /−55.3	11.7 /−79.0	11.6 /−65.5	0.60/−68.9	0.62/−47.5	0.61/−28.2
5.42/−40.0	5.77/−59.0	6.27/<−79.3	5.58/−70.7		0.21/−59.8	0.22/−37.0
0.60/−55.8	0.67/<−79.3				0.05/<−79.3	0.08/−45.3
				0.43/>−79.3		0.04/−53.3
				0.12/<−79.3		0.01/−69.0

Myristyl alcohol	Palmityl alcohol	Stearyl alcohol	Oleyl alcohol	Linoleyl alcohol	Linolenyl alcohol	Tricaprylin
6.22/8.0	7.13/22.4	1.07/18.6	11.8 /12.7	27.2 /−25.0	25.0 /−38.9	19.63/−15.9
2.22/1.0	5.51/19.1	0.43/10.8	5.41/−17.8	11.1 /−28.6	11.1 /−44.0	12.74/−18.3
0.94/−6.5	2.67/14.2	0.16/3.3	2.66/−23.1	5.32/−33.3	5.48/−49.1	6.61/−21.8
0.35/−13.8	2.08/12.0	0.07/−1.7	1.05/−29.5	2.62/−37.8	2.69/−55.1	4.42/−24.3
0.15/−20.8	1.00/8.3	0.03/−16.0	0.55/−34.8	1.04/−45.7	1.05/−63.9	2.63/−27.3
0.05/−31.6	0.82/7.1	0.01/>−79.3	0.25/−41.9	0.54/−50.8	0.54/−71.0	1.06/−32.7
0.02/−37.1	0.31/0.9		0.12/−47.5	0.11/−63.3	0.18/<−79.3	
0.01/−46.5	0.126/−6.0					
	0.05/−12.2					

Tricaprin	Trilaurin	Trimyristin	Triolein	Trilinolein	Trilinolenin	
5.41/1.8	5.21/21.5	0.43/24.7	185.7 /−3.8	25.0 /−25.0	99.8 /−38.0	
2.88/−1.5	2.65/18.0	0.11/18.5	64.2 /−4.0	11.48/−26.0	42.7 /−39.1	
1.06/−8.0	1.04/13.8	0.06/16.3	25.3 /−4.5	2.28/−30.7	11.5 /−40.3	
0.51/−13.0	0.51/10.3		8.32/−6.5	0.54/−37.0	5.52/−43.3	
0.21/−19.5	0.23/6.5		1.20/−11.8	0.22/−40.7	2.11/−47.0	
0.10/−21.8	0.11/3.3		0.52/−14.8	0.05/−47.3	1.11/−50.7	
			0.20/−18.5			
			0.05/−25.5			

[a] Calculated values.

unreacted methyl ester were removed by extraction of a Skellysolve F solution of the compounds with 80% aqueous ethanol. The washed products then were crystallized from acetone, Skellysolve F, or diethyl ether.

The triglycerides of the lower saturated acids were prepared by direct esterification with glycerol, using p-toluenesulfonic acid as catalyst. The crude tricaproin and tricaprylin were purified by high-vacuum distillation. Tricaprylin, tricaprin, and trilaurin were further purified by several recrystallizations from acetone. Saponification values were as follows: tricaproin 417.8; tricaprylin 348.3; tricaprin 302.4; trilaurin 263.5; trimyristin 235.9; tripalmitin 208.9; tristearin 189.9. Other analytical data on the saturated triglycerides are given in Table I. Triolein had an iodine value of 86.0, n_D^{30} 1.4638; trilinolein, an iodine value of 171.0, n_D^{25} 1.4750; trilinolenin, an iodine value of 260.4, n_D^{40} 1.4825.

Apparatus and Procedure

The apparatus devised for the solubility measurements in this study is shown in Figure 1 and has been described elsewhere (10). It was virtually identical with an apparatus devised by Ward and Singleton, a description of which was published during the course of the work presented here (11). However, as mentioned previously, in our work the solubility end-point was approached from the cold side.

Although, as shown by Ward and Singleton (11), the end-point may be approached from the warm side with some materials such as 1-monostearin, this approach was found to be impractical with some of the compounds in our study because of difficulties caused by supercooling and polymorphism. In our hands the results of the synthetic method were in no way impaired by visual detection of the end-point as approached from the cold side. The temperature at which complete solution occurred was reproducible in most cases within ± 0.1°C.
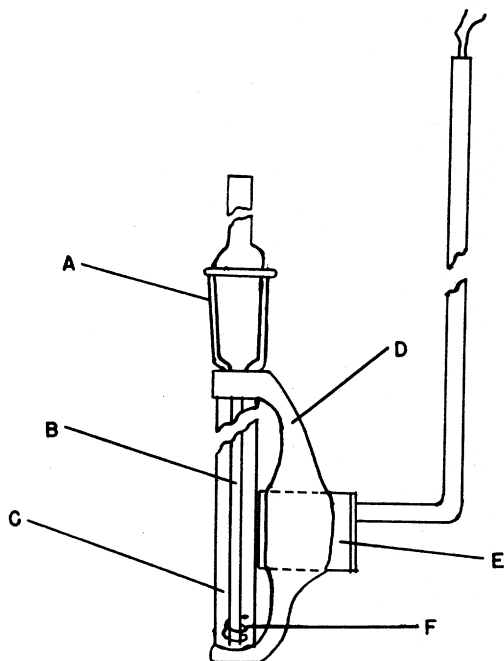

FIG. 1. Solubility apparatus: A, 14/35 ground glass joint; B, thermocouple well; C, crystallization chamber; D, support; E, small solenoid; F, tin-plated iron coil.

Detection of the total disappearance of crystals was greatly facilitated by observations through a strong magnifying glass and by illumination from a pinpoint light source (12 v. AC-DC "grain of wheat" bulb), placed directly behind the sample chamber.

With each compound a series of solutions was prepared at concentrations selected to provide adequate data for the accurate construction of its solubility curve. An individual sample chamber containing about 2 ml. of solution was used for each concentration. In general, it was found convenient to conduct measurements in an order progressing from the lowest to the highest concentrations.

In each case the solution was cooled to a temperature where an appreciable number of crystals formed. It then was placed in a support and immersed in an acetone bath, the temperature of which was about the same as that of the sample. Cooling of the acetone bath was accomplished by immersing several cold elements consisting of Pyrex cylinders that contained dry ice. The bath was equipped with a stirrer to maintain a uniform temperature throughout.

The rate of warming of the bath was controlled by removing one or more of the cold elements from time to time. A magnetically operated agitator in the solution provided rapid heat distribution and thorough mixing of the solution and crystals. The temperature was allowed to rise about 1°C. per 5 minutes more or less, depending to some extent on the solubility and the temperature coefficient of solubility. Preliminary experiments indicated that this rate of temperature rise was sufficiently small so that virtual equilibrium existed at the time when the last crystals disappeared.

The temperature of the solution was measured with a calibrated, single element thermocouple constructed from No. 30 B & S ga. copper and constantan wires. The thermocouple voltage was measured with a Leeds and Northrup K-2 potentiometer used in conjunction with a Leeds and Northrup No. 2430 galvanometer. With this system, temperatures were determined with an accuracy of ± 0.1°C. over the temperature ranges studied.

The same procedure was used with each succeeding solution of higher concentration until the temperature range up to the melting point of the compound had been covered. The solubilities are presented in tabular form (Table II). Figure 2 compares the data obtained for linoleic acid by our method with those reported by Foreman and Brown (4), Kolb and Brown (6), and Hoerr and Harwood (5).

Where reliable data had previously been obtained by others, only scattered determinations were made in this study, primarily as a check on the method employed here. In most cases the results of this study agree well with the data previously obtained (Figure 2).

The preparation of methyl caproate could not be crystallized from acetone at −70°C., and the solubility values for this compound are hypothetical, obtained by extrapolation of the solubilities of the other members of the series.

The solubility of tristearin was less than 0.025% at 40°C., and the solubility of tripalmitin was only 0.027% at 24°C.

Although most fatty materials exhibit more than one crystal modification, it is generally believed that only the most stable polymorph is formed by crys-
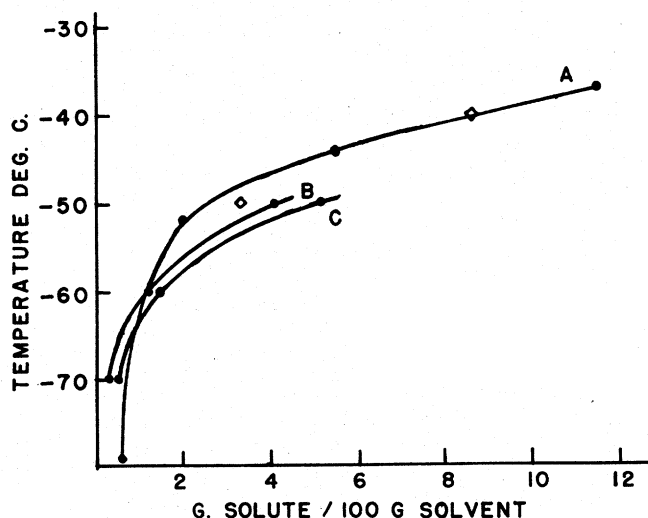
FIG. 2. Solubility of linoleic acid in acetone as obtained by different investigators: A, authors (synthetic method); B, Kolb, D. K., and Brown, J. B. (3, 6) (analytical method); C, Foreman, H. B., and Brown, J. B. (4) (analytical method); □ Hoerr, C. W., and Harwood, H. S. (5) (synthetic method).

tallization from common fat solvents. Such was not the case with some of the compounds in this study. Because different polymorphs of the same substance have different solubilities, as has been observed with oleic acid, for example, by Hoerr and Harwood (5), it was necessary to use special precautions in some cases to insure that the solubilities of the stable forms were being determined.

A good example of the effect of polymorphism on solubility encountered in this work was represented by the case of palmityl alcohol in hexane. The solubility depended on the previous history of the palmityl alcohol, the crystallization procedure used, and the conditioning of the sample. Palmityl alcohol previously crystallized from hexane or benzene gave entirely different solubility data than when crystallized from acetone unless the samples were properly conditioned.

In general, whenever this problem was encountered, it was necessary to treat each case individually and to find by trial and error the conditions that would give crystals in their most stable modification.

The data obtained here extend the information on the solubilities of the fatty acids and derivatives that were studied and may be used as a guide for separation of mixtures by crystallization procedures. However, with mixtures of fatty acids in solution, the solubility of any given fatty acid is affected by the solubilizing effect of other fatty acids in the mixture, and the nature and extent of this solubilizing effect is also dependent on the nature of the solvent. Because of a paucity of data on the solubility characteristics of mixtures, it would be desirable to follow these measurements of pure individual compounds with studies of model mixtures. Nevertheless the solubility curves for the pure compounds are useful, even when fractional crystallization of mixtures is contemplated, and can be used in selecting solvents, solute concentrations, and crystallization temperatures.

Summary

An improved "synthetic" method of determining solubilities has been described which combines simplicity with accuracy.

Saturated fatty acids with even numbers of carbons from C_6 to C_{18} and oleic, linoleic, and linolenic acids, their methyl esters, their simple triglycerides, and their corresponding alcohols have been prepared in purified form. The solubilities in acetone of their most stable forms have been determined from ordinary room temperatures down to about $-70°C$. or to temperatures where they are only slightly soluble.

The precipitation of unstable polymorphs from solutions was observed in the case of palmityl alcohol.

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